

### **REMARKS / ARGUMENTS**

Claims 37-80 are currently pending in the application. Claims 69 and 75-80 have been rejected. Claims 70-72 have been objected to. Claims 37-68 have been cancelled herein as being drawn to non-elected subject matter. However, Applicants reserve the right to pursue the subject matter of these claims, or related subject matter, in a future continuation or divisional application. While the Examiner has failed to indicate the status of pending claims 73-74 (“withdrawn” or “under consideration”), for the purposes of this Response, Applicants are assuming these claims have been withdrawn from consideration. Applicants respectfully request clarification from the Examiner. Additionally, Applicants gratefully acknowledge the Examiner’s removal of the restriction requirement and the rejoining of 69-72 and 75-80.

Applicants have amended claims 69, 71, 77 and 78, cancelled claims 37-68, 76, 79 and 80, and added new claims 81-106 herein. No new matter has been added by way of these amendments. Claim 69 has been amended to incorporate all of the limitations of dependent claim 76, which has been cancelled herein. Support for the recitation of “identity” in claims 69 and 77, can be found at page 21, lines 11-20. Support for the recitation of “greater than 80%” identity in claim 69 can be found on page 21, line 25. Claim 71 has been amended to correct a minor typographical error (“PPYX” changed to “PPXY”), for which support can be found on page 13, line 23. Claim 78 has been re-written in independent form. New claims 81, 88 and 92 parallel the language used in claim 70, but do not recite “in a host cell.” New claims 82-84 have been added and parallels the language used in claims 70-72. New claims 85, 89, 93 recite that the Smurf activity is ubiquitination of a TGF $\beta$  for which support can be found, for example, on page 64, line 30 - page 65, line 13. New claims 86, 90, 94, 95, and 100 recite that the screening assay is conducted *in vitro*, and support can be found throughout the specification, *e.g.*, at page 43, lines 7-29. New claims 87, 91, 96 and 101 recite that the screening assay is conducted in a host cell, and new claims 102-106 recite that the screening assay is conducted *in vivo*. Support for new claims 87, 91, 96, 101-106 can be found throughout the specification, *e.g.*, at page 43, line 30 - page 44, line 25.

Applicants gratefully acknowledge the Examiner's recognition of the allowability of claims 70-72, if rewritten in independent form (Office Action, page 11). As such, new claims 97-99 have been added.

Following entry of this amendment, claims 69-72, 75, 77, 78, and 81-106 will be pending in this application. Applicants respectfully request reconsideration of pending claims 69-72, 75, 77, 78, and 81-106.

**I. Objection to the Specification**

Applicants have amended the specification to capitalize trademarks, when appropriate, and to remove hyperlink text. Applicants have also revised the title of the application, as suggested by the Examiner. No new matter has been added by way of this amendment.

Accordingly, Applicants respectfully request that these objections to the specification be reconsidered and withdrawn.

**II. Objection to the Drawings**

**A. Brief Description of the Drawings**

The Examiner has objected to the Drawings because the Brief Description of the Drawings on pages 5-13 was "not accurate" (Office Action, page 5). As suggested by the Examiner, Applicants have amended the specification to include the various Figure "parts." For example, Applicants have amended the description of Figure 9 to refer to parts A-F, *etc.* No new matter has been added by way of this amendment.

**B. "Blurry" Figure 2**

The Examiner has also objected to the Drawings "because some of the figures are blurry, see for example Figure 2" (Office Action, page 5).

Applicants respectfully traverse this ground of objection.

Applicants respectfully submit that Figure 2 (as well as all of the other Figures) are clear. As the Examiner is aware, Northern blots, and other types of blots and gels, inherently produce a somewhat “blurry” appearance. Notwithstanding, in Figure 2A, for example, the 6 kb transcript can clearly be seen in each tested stage of embryonic development (lanes 1-3). Similarly, Figure 2B clearly shows the 6 kb transcript in each of the tissues tested (except in muscle (M)), with only low levels of transcript being seen in spleen (Sp) and kidney (K) and higher levels being seen in each of the other tested tissues. Figure 2B also shows abundant expression of the 3 kb transcript in testes (T), and very weak or no expression in the kidney, lung, spleen, brain and heart. These data are entirely consistent with the description of the results shown in Figures 2A and 2B discussed on page 50 of the specification.

Thus, Applicants submit that Figure 2 (as well as the other Drawings filed on December 11, 2001) complies with all of the requirements of 37 C.F.R. § 1.121(d). Besides Figure 2, the Examiner has not indicated exactly which other Figures (if any) of the 47 sheets of Drawings in this application are objected to as being “blurry.” If necessary, Applicants respectfully request additional clarification from the Examiner.

In view of the foregoing, Applicants respectfully submit that Figure 2, as well as each of the other Figures in the Drawings of the above-referenced application, are not “blurry” and comply with all of the requirements of 37 C.F.R. 1.121(d).

Accordingly, Applicants respectfully request that this ground of objection be reconsidered and withdrawn.

### **III. Information Disclosure Statement**

As requested by the Examiner, Applicants submit herewith duplicate copies of the eighty-five (85) non-patent publications (labelled AF-DL) originally filed on January 10, 2003. Acknowledgement and consideration of these non-patent publications listed on the

PTO-Form 1449 filed on January 10, 2003 (copy enclosed for Examiner's convenience) is respectfully requested.

**IV. Rejection Under 35 U.S.C. § 112, First Paragraph.**

The Examiner has rejected claims 76-77 and 79-80 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed.

Applicants respectfully traverse this ground of rejection.

It is noted that claims 76 and 79-80 have been cancelled herein. However, claim 69 has been amended to essentially recite all the limitations of cancelled claim 76. Accordingly, the arguments herein refer to claims 69 and 77, as amended herein.

First, the Examiner alleges that "the claimed invention is directed to Smurf activity of a Smurf comprising greater than 70% or 90% homology with the amino acid sequence depicted in SEQ ID NO:2 and a Smurf activity of a Smurf comprising greater than 70% or 90% homology with the amino acid sequence depicted in SEQ ID NO:4" (Office Action, page 7; emphasis added). Respectfully, this statement is inaccurate. In fact, the pending claims are drawn to methods of screening for a modulator of Smurf activity.

The Examiner has expressed concerns over the use of a percent "homology" with a given SEQ ID NO. Solely in an effort to advance prosecution of this application, Applicants have amended claims 69 and 77 to recite a percent "identity" with SEQ ID NO:2.

The Examiner opines that the "genus of the polypeptides encompassed by the claims is highly variable" and that the specification "fails to provide any additional representative species of the claimed genus to show that the applicant was in possession of the claimed genus" (Office Action, page 7). First, it is noted that claim 78, as amended recites that the Smurf comprises the sequence depicted in SEQ ID NO:4. With respect to the 80% and 90% sequence identity requirements of claims 69 and 77, respectively, Applicants submit that one

skilled in the art could readily envision each and every species of the claimed genus based on its relative identity to a definite structural feature: SEQ ID NO:2.

M.P.E.P § 2164.01 states that 35 U.S.C. § 112, first paragraph, “has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation.” The same section further states that “[t]he fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation.”

Applicants submit that one of ordinary skill in the art would know how to identify and utilize Smurf polypeptides for use in the methods of the invention without undue experimentation. For example, the specification provides extensive guidance as to how to clone Smurf family genes (*e.g.*, at pages 23-24) and express Smurf family proteins (*e.g.*, at pages 27-39). The Examiner is also directed to Example 1, wherein human, mouse and *Xenopus* Smurf1 were identified, and to Example 2, wherein human and mouse Smurf2 were identified using techniques disclosed in the specification and well-known in the art. Additionally, the specification provides extensive guidance at pages 24-27 as to how to obtain Smurf derivatives (*e.g.*, insertions, deletions, substitutions, *etc.*), using techniques well-known to skilled artisans at the time the application was filed (*see, e.g.*, Sambrook *et al.*, 1989, cited on page 26, line 29 of the specification) Further, the specification provides additional guidance at pages 41-46 as to how to use the Smurf family proteins in various routine *in vitro* and *in vivo* screening assays.

The Examiner further opines that the “claimed genus of polypeptides could include non-functional proteins or proteins with a different function than the one described” (Office Action, page 8). However, the Examiner is respectfully reminded that even if some of the species in a genus claim are inoperative, the claims are not necessarily invalid. *Atlas Powder Co. v. E.I. Du Pont de Nemours & Co.*, 750 F.2d 1569, 1576; 224 U.S.P.Q. (BNA) 409. “It is not a function of the claims to specifically exclude...possible inoperative substances....” *Id.* (citing *In re Dinh-Nguyen*, 492 F.2d 856, 858-59, 181 U.S.P.Q. (BNA) 46, 48 (CCPA 1974) (emphasis omitted); accord, *In re Geerdes*, 491 F.2d 1260, 1265, 180 U.S.P.Q. (BNA) 789, 793 (CCPA 1974); *In re Anderson*, 471 F.2d 1237, 1242, 176 U.S.P.Q. (BNA) 331, 334-35 (CCPA 1973)). However, it was routine at the time the application was filed to screen large

amounts of mutants, for example in high-throughput screening assays, for functional activity.

Thus, Applicants submit that the specification clearly conveys to one having skill in the art that they were in possession of the claimed invention. Accordingly, reconsideration and withdrawal of this ground of rejection is respectfully requested.

**V. Rejection Under 35 U.S.C. § 102(b)**

Claims 69, 75-76 and 78-80 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Beach *et al.* (WO 97/12962) (“Beach”) (Office Action, pages 9-10).

Applicants respectfully traverse this ground of rejection.

It is noted that claims 76 and 79-80 have been cancelled herein, thus rendering rejection of these claims moot.

The Examiner contends that because the claims “merely requires the activity of the sequence and not the sequence *per se*,” Beach anticipates these claims (Office Action, page 10). For example, the Examiner opines Beach anticipates claim 75, which recites that the Smurf comprises SEQ ID NO:2, because Beach allegedly teaches a sequence with 77% identity to SEQ ID NO:2 that has E3 ubiquitin ligase activity (“the Beach sequence”). However, the fact that the Beach sequence may contain E3 ubiquitin ligase activity is irrelevant to the novelty of claim 75 because the Beach sequence does not comprise SEQ ID NO:2, as required by claim 75. Thus, Beach does not anticipate claim 75.

Similar arguments can be made with respect to independent claims 69 and 78. Claim 69, as amended herein, recites that the Smurf activity detected is the activity of a Smurf comprising greater than 80% identity with the amino acid sequence depicted in SEQ ID NO:2. Beach does not teach a sequence that is greater than 80% identity with the amino acid sequence depicted in SEQ ID NO:2, much less teach a method of screening for a modulator of Smurf activity which comprises detecting modulation of activity of a Smurf that comprises greater than 80% identity with the amino acid sequence depicted in SEQ ID NO:2. Thus,

Beach does not anticipate independent claim 69 (or dependent claims 70-73 and 75, which depend therefrom).

Similarly, Beach also does not teach a method of screening for a modulator of Smurf activity which comprises detecting modulation of activity of a Smurf that comprises the amino acid sequence depicted in SEQ ID NO:4. Thus, Beach does not anticipate independent claim 78 (or dependent claims 81-83, which depend therefrom).

Thus, Applicants submit that Beach does not anticipate any of pending claims 69, 75, 77 or 78, as amended herein. Beach also does not anticipate any of new claims 81-106. Accordingly, reconsideration and withdrawal of this ground of rejection is respectfully requested.

## **VI. Conclusion**

In view of the foregoing remarks, Applicants respectfully submit that this application is now in condition for allowance. If a telephone interview would advance prosecution of the application, the Examiner is invited to call the undersigned at the number listed below.

A Petition for a two (2) month Extension of Time under 37 C.F.R. § 1.136(a) is filed concurrently herewith, which extends the response period from January 6, 2005 to March 6, 2005. Because March 6, 2005 falls on a Sunday, the response period is extended to Monday, March 7, 2005, pursuant to 37 C.F.R. § 1.7. The Petition further authorizes the PTO to charge the two month extension fee of \$450 to our Deposit Account No. 50-3013. Applicants believe no other fees are due in connection with this Amendment. However, if there are any other fees due, please charge them to Deposit Account 50-3013. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above or in the Petition filed concurrently herewith, such an extension is requested and the fee should be charged to our

Deposit Account. Also, please charge any fees underpaid or credit any fees overpaid to the same Deposit Account.

Respectfully submitted,

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